

We claim:

1. A method of making a transgenic avian lacking expression of endogenous immunoglobulin, comprising:

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inactivating at least one endogenous heavy chain immunoglobulin locus in at least one avian cell;

generating at least one avian from said at least one avian cell; and

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optionally breeding said at least one avian to obtain a transgenic avian lacking expression of endogenous immunoglobulins.

2. The method of claim 1, further comprising introducing at least a portion of at least one exogenous immunoglobulin locus into at least one avian cell.

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3. The method of claim 2, wherein said at least a portion of said at least one exogenous immunoglobulin locus comprises at least a portion of at least one heavy chain constant region.

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4. The method of claim 3, wherein said at least one heavy chain constant region is a human heavy chain constant region.

5. The method of claim 3, wherein said at least a portion of at least one exogenous immunoglobulin locus comprises at least a portion of the V_H , D_H , J_H , and C_H regions.

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6. The method of claim 1, further comprising inactivating at least one endogenous immunoglobulin light chain locus in at least one avian cell.

7. The method of claim 6, further comprising introducing at least a portion of at least one exogenous immunoglobulin light chain locus into at least one avian cell.

8. The method of claim 7, wherein said at least a portion of at least one exogenous immunoglobulin light chain locus is at least a portion of at least one human immunoglobulin light chain locus.

9. The method of claim 7, wherein said at least a portion of at least one exogenous immunoglobulin light chain locus comprises at least a portion of at least one light chain constant region.

10. The method of claim 7, wherein said at least a portion of at least one exogenous immunoglobulin light chain locus comprises at least a portion of the V_L , J_L , and C_L regions.

11. The method of claim 1, wherein said avian cell is a chicken cell, a turkey cell, a duck cell, a goose cell, or a quail cell.

12. A method of making a chimeric antibody, comprising:

immunizing the transgenic avian of claim 3 with an antigen;

5 harvesting serum or obtaining at least one egg from said transgenic avian; and

isolating at least one chimeric antibody or at least one exogenous antibody from said serum or said at least one egg.

- 10 13. An antibody made by the method of claim 12.

14. A method of making a chimeric monoclonal antibody, comprising:

immunizing the transgenic avian of claim 3 with an antigen;

15 harvesting B cells from said transgenic avian;

immortalizing said B cells; and

20 isolating at least one monoclonal antibody from the culture medium of said B cells.

15. An antibody made by the method of claim 14.

16. A method of making a xenogenic antibody, comprising:

immunizing the transgenic avian of claim 10 with an antigen;

5 harvesting serum or obtaining at least one egg from said transgenic avian; and

isolating at least one xenogenic antibody from said serum or said at least one egg.

17. An antibody made by the method of claim 16.

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18. A method of making a xenogenic monoclonal antibody, comprising:

immunizing the transgenic avian of claim 10 with an antigen;

15 harvesting B cells from said transgenic avian;

immortalizing said B cells; and

isolating at least one monoclonal antibody from the culture medium of said B cells.

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19. An antibody made by the method of claim 18.

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20. The method of claim 18, further comprising:

isolating at least one nucleic acid molecule comprising cDNA encoding at least a portion of an immunoglobulin from said immortalized B cells;

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introducing said at least one nucleic acid molecule comprising cDNA encoding at least a portion of an immunoglobulin into at least one other cell;

culturing said at least one other cell under conditions that promote protein synthesis;

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and

isolating at least one antibody from the culture medium of said at least one other cell.

21. The method of claim 20, wherein said at least one other cell is at least one prokaryotic, fungal, avian or mammalian cell.

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22. An antibody made by the method of claim 20.

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